ds

Set	Items	Description
S1	5607	ARRESTIN
S2	9	ARRESTING AND GPCR
S3	426	ARRESTIN AND GPCR
S4	333	S3 AND (KINASE OR PHOSPHOR?)
S5	19	S4 AND DETECT?
S6	14	RD (unique items)

AMJ 9/21/02

?t 6/3,ab/1-14
>>>No matching display code(s) found in file(s): 65, 135

6/3,AB/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13669681 BIOSIS NO.: 200200298502
Differences in the cellular localization and agonist-mediated internalization properties of the alpha1-adrenoceptor subtypes.
AUTHOR: Chalothorn Dan; McCune Dan F; Edelmann Stephanie E; Garcia-Cazarin Mary L; Tsujimoto Gozoh; Piascik Michael T(a)
AUTHOR ADDRESS: (a)Department of Molecular and Biomedical Pharmacology, University of Kentucky College of Medicine, 800 Rose Street, Lexington, KY, 40536-0084**USA E-Mail: mtp@uky.edu
JOURNAL: Molecular Pharmacology 61 (5):p1008-1016 May, 2002
MEDIUM: print
ISSN: 0026-895X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The cellular localization, agonist-mediated internalization, and desensitization properties of the alpha1-adrenoceptor (alpha1-AR) subtypes conjugated with green fluorescent protein (alpha1-AR/GFP) were assessed using real-time imaging of living, transiently transfected human embryonic kidney (HEK) 293 cells. The alpha1B-AR/GFP fluorescence was **detected** predominantly on the cell surface. Stimulation of the alpha1B-AR with phenylephrine led to an increase in extracellular signal-regulated **kinase** 1/2 (ERK1/2) **phosphorylation** and promoted rapid alpha1B-AR/GFP internalization. Long-term exposure (15 h) to phenylephrine resulted in desensitization of the alpha1B-AR-mediated activation of ERK1/2 **phosphorylation** . alpha1A-AR/GFP fluorescence was **detected** not only on the cell surface but also intracellularly. The rate of internalization of the cell surface population alpha1A-AR/GFPs was slower than that seen for the alpha1B-AR. Agonist exposure also resulted in desensitization of the alpha1A-AR-mediated increase in ERK1/2 **phosphorylation** . The alpha1D-AR/GFP fluorescence was **detected** mainly intracellularly, and this localization was unaffected by exposure to phenylephrine. Phenylephrine treatment of alpha1D-AR/GFP expressing cells increased ERK1/2 **phosphorylation** . However, this increase was not significant. Cotransfection with beta- **arrestin** 1 did not increase the rate or extent of agonist-stimulated alpha1A- or alpha1B-AR/GFP internalization. However, a dominant-negative form of the beta- **arrestin** 1, beta- **arrestin** 1 (319-418), blocked agonist-mediated internalization of both the alpha1A- and alpha1B-ARs. These data show that transfected alpha1-AR/GFP fusion proteins are functional, that there are differences in the cellular distribution and agonist-mediated internalization between the alpha1-ARs, and that agonist-mediated alpha1-AR internalization is dependent on arrestins and can be desensitized by long-term exposure to an agonist. These differences could contribute to the diversity in physiologic responses regulated by the alpha1-ARs.

2002

6/3,AB/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13626080 BIOSIS NO.: 200200254901
Conservation of the phosphate-sensitive elements in the arrestin **family of proteins.**
AUTHOR: Celver Jeremy; Vishnivetskiy Sergey A; Chavkin Charles; Gurevich Vsevolod V(a)
AUTHOR ADDRESS: (a)Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, TN, 37232**USA E-Mail: Vsevolod.Gurevich@mcmail.vanderbilt.edu
JOURNAL: Journal of Biological Chemistry 277 (11):p9043-9048 March 15, 2002
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Arrestins play a key role in the homologous desensitization of G protein-coupled receptors (GPCRs). These cytosolic proteins selectively bind to the agonist-activated and **GPCR kinase - phosphorylated** forms of the **GPCR** , precluding its further interaction with the G protein. Certain mutations in visual **arrestin** yield "constitutively active" proteins that bind with high affinity to the light-activated form of rhodopsin without requiring **phosphorylation** . The crystal structure of visual **arrestin** shows that these activating mutations perturb two groups of intramolecular interactions that keep **arrestin** in its basal (inactive) state. Here we introduced homologous mutations into arrestin2 and arrestin3 and found that the resulting mutants bind to the beta2-adrenoreceptor in vitro in a **phosphorylation** -independent fashion. The same mutants effectively desensitize both the beta2-adrenergic and delta-opioid receptors in the absence of receptor **phosphorylation** in Xenopus oocytes. Moreover, the **arrestin** mutants also desensitize the truncated delta-opioid receptor from which the C terminus, containing critical **phosphorylation** sites, has been removed. Conservation of the phosphate-sensitive hot spots in non-visual arrestins suggests that the overall fold is similar to that of visual **arrestin** and that the mechanisms whereby receptor-attached phosphates drive **arrestin** transition into the active binding competent state are conserved throughout the **arrestin** family of proteins.

2002

6/3,AB/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13349595 BIOSIS NO.: 200100556744
Cell-type specific effects of endocytosis inhibitors on 5-hydroxytryptamine2A receptor desensitization and resensitization reveal an arrestin **-, GRK2-, and GRK5-independent mode of regulation in human embryonic kidney 293 cells.**
AUTHOR: Gray John A; Sheffler Douglas J; Bhatnagar Anushree; Woods Jason A; Hufeisen Sandra J; Benovic Jeffrey L; Roth Bryan L(a)
AUTHOR ADDRESS: (a)Department of Biochemistry, Case Western Reserve University School of Medicine, 10900 Euclid Ave., Room W438, Cleveland, OH, 44106-4935: roth@biocserver.cwru.edu**USA
JOURNAL: Molecular Pharmacology 60 (5):p1020-1030 November, 2001
MEDIUM: print
ISSN: 0026-895X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The effect of endocytosis inhibitors on 5-hydroxytryptamine2A

(5-HT2A) receptor desensitization and resensitization was examined in transiently transfected human embryonic kidney (HEK) 293 cells and in C6 glioma cells that endogenously express 5-HT2A receptors. In HEK-293 cells, 5-HT2A receptor desensitization was unaffected by cotransfection with a dominant-negative mutant of dynamin (DynK44A), a truncation mutant of **arrestin** -2 (Arr2(319-418)), or by two well-characterized chemical inhibitors of endocytosis: concanavalin A (conA) and phenylarsine oxide (PAO). In contrast, beta2-adrenergic receptor desensitization was significantly potentiated by each of these treatments in HEK-293 cells. In C6 glioma cells, however, DynK44A, Arr2(319-418), conA, and PAO each resulted in the potentiation of 5-HT2A and beta-adrenergic receptor desensitization. The cell-type-specific effect of Arr2(319-418) on 5-HT2A receptor desensitization was not related to the level of GRK2 or GRK5 expression. Interestingly, although beta2-adrenergic receptor resensitization was potently blocked by cotransfection with DynK44A, 5-HT2A receptor resensitization was enhanced, suggesting the existence of a novel cell-surface mechanism for 5-HT2A receptor resensitization in HEK-293 cells. In addition, Arr2(319-418) had no effect on 5-HT2A receptor resensitization in HEK-293 cells, although it attenuated the resensitization of the beta2-adrenergic receptor. However, in C6 glioma cells, both DynK44A and Arr2(319-418) significantly reduced 5-HT2A receptor resensitization. Taken together, these results provide the first convincing evidence of cell-type-specific roles for endocytosis inhibitors in regulating **GPCR** activity. Additionally, these results imply that novel GRK and **arrestin** -independent mechanisms of 5-HT2A receptor desensitization and resensitization exist in HEK-293 cells.

2001

6/3,AB/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12432917 BIOSIS NO.: 200000186419
Enhanced morphine analgesia in mice lacking beta- arrestin **2.**
AUTHOR: Bohn Laura M; Lefkowitz Robert J; Gainetdinov Raul R; Peppel Karsten; Caron Marc G(a); Lin Fang-Tsyr
AUTHOR ADDRESS: (a)Departments of Cell Biology and Medicine, Howard Hughes Medical Institute Laboratories, Duke University Medical Center, Durham, NC, 27710**USA
JOURNAL: Science (Washington D C) 286 (5449):p2495-2498 Dec. 24, 1999
ISSN: 0036-8075
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The ability of morphine to alleviate pain is mediated through a heterotrimeric guanine nucleotide binding protein (G protein)-coupled heptahelical receptor (**GPCR**), the mu opioid receptor (muOR). The efficiency of **GPCR** signaling is tightly regulated and ultimately limited by the coordinated **phosphorylation** of the receptors by specific **GPCR** kinases and the subsequent interaction of the **phosphorylated** receptors with beta- **arrestin** 1 and beta- **arrestin** 2. Functional deletion of the beta- **arrestin** 2 gene in mice resulted in remarkable potentiation and prolongation of the analgesic effect of morphine, suggesting that muOR desensitization was impaired. These results provide evidence in vivo for the physiological importance of beta- **arrestin** 2 in regulating the function of a specific **GPCR** , the muOR. Moreover, they suggest that inhibition of beta- **arrestin** 2 function might lead to enhanced analgesic effectiveness of morphine and provide potential new avenues for the study and treatment of pain, narcotic tolerance, and dependence.

1999

6/3,AB/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12260203 BIOSIS NO.: 200000013705
Properties of secretin receptor internalization differ from those of the beta2-adrenergic receptor.
AUTHOR: Walker Julia K L; Premont Richard T; Barak Larry S; Caron Marc G(a) ; Shetzline Michael A
AUTHOR ADDRESS: (a)Duke University Medical Center, Durham, NC, 27710**USA
JOURNAL: Journal of Biological Chemistry 274 (44):p31515-31523 Oct. 29, 1999
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The endocytic pathway of the secretin receptor, a class II **GPCR** , is unknown. Some class I G protein-coupled receptors (GPCRs), such as the beta2-adrenergic receptor (beta2-AR), internalize in clathrin-coated vesicles and this process is mediated by G protein-coupled receptor kinases (GRKs), beta- **arrestin** , and dynamin. However, other class I GPCRs, for example, the angiotensin II type 1A receptor (AT1AR), exhibit different internalization properties than the beta2-AR. The secretin receptor, a class II **GPCR** , is a GRK substrate, suggesting that like the beta2-AR, it may internalize via a beta- **arrestin** and dynamin directed process. In this paper we characterize the internalization of a wild-type and carboxyl-terminal (COOH-terminal) truncated secretin receptor using flow cytometry and fluorescence imaging, and compare the properties of secretin receptor internalization to that of the beta2-AR. In HEK 293 cells, sequestration of both the wild-type and COOH-terminal truncated secretin receptors was unaffected by GRK **phosphorylation** , whereas inhibition of cAMP-dependent protein **kinase** mediated **phosphorylation** markedly decreased sequestration. Addition of secretin to cells resulted in a rapid translocation of beta- **arrestin** to plasma membrane localized receptors; however, secretin receptor internalization was not reduced by expression of dominant negative beta- **arrestin** . Thus, like the AT1AR, secretin receptor internalization is not inhibited by reagents that interfere with clathrin-coated vesicle-mediated internalization and in accordance with these results, we show that secretin and AT1A receptors colocalize in endocytic vesicles. This study demonstrates that the ability of secretin receptor to undergo GRK **phosphorylation** and beta-**arrestin** binding is not sufficient to facilitate or mediate its internalization. These results suggest that other receptors may undergo endocytosis by mechanisms used by the secretin and AT1A receptors and that kinases other than GRKs may play a greater role in **GPCR** endocytosis than previously appreciated.

1999

6/3,AB/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11219535 BIOSIS NO.: 199800000867
A beta- arrestin **/green fluorescent protein biosensor for** detecting **G protein-coupled receptor activation.**
AUTHOR: Barak Larry S; Ferguson Stephen S G; Zhang Jie; Caron Marc G(a)
AUTHOR ADDRESS: (a)Duke Univ. Med. Cent., Box 3287, Durham, NC 27710**USA
JOURNAL: Journal of Biological Chemistry 272 (44):p27497-27500 Oct. 31, 1997
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: G protein-coupled receptors (**GPCR**) represent the single most important drug targets for medical therapy, and information from genome sequencing and genomic data bases has substantially accelerated their discovery. The lack of a systematic approach either to identify the function of a new **GPCR** or to associate it with a cognate ligand has added to the growing number of orphan receptors. In this work we provide a novel approach to this problem using a beta-arrestin2/green fluorescent protein conjugate (betaarr2-GFP). It provides a real-time and single cell based assay to monitor **GPCR** activation and **GPCR** -G protein-coupled receptor **kinase** or **GPCR** - **arrestin** interactions. Confocal microscopy demonstrates the translocation of betaarr2-GFP to more than 15 different ligand-activated GPCRs. These data clearly support the common hypothesis that the beta- **arrestin** binding of an activated receptor is a convergent step of **GPCR** signaling, increase by 5-fold the number of GPCRs known to interact with beta-arrestins, demonstrate that the cytosol is the predominant reservoir of biologically active beta-arrestins, and provide the first direct demonstration of the critical importance of G protein-coupled receptor **kinase** **phosphorylation** to the biological regulation of beta- **arrestin** activity and **GPCR** signal transduction in living cells. The use of betaarr2-GFP as a biosensor to recognize the activation of pharmacologically distinct GPCRs should accelerate the identification of orphan receptors and permit the optical study of their signal transduction biology intractable to ordinary biochemical methods.

1997

6/3,AB/7 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

06986581 Genuine Article#: 111VM Number of References: 42
Title: Differential expression of alternative splice variants of beta-arrestin -1 and -2 in rat central nervous system and peripheral tissues
(ABSTRACT AVAILABLE)
Author(s): Komori N (REPRINT) ; Cain SD; Roch JM; Miller KE; Matsumoto H
Corporate Source: UNIV OKLAHOMA,HLTH SCI CTR, DEPT BIOCHEM & MOL BIOL/OKLAHOMA CITY//OK/73190 (REPRINT); UNIV OKLAHOMA,HLTH SCI CTR, DEPT CELL BIOL/OKLAHOMA CITY//OK/73190
Journal: EUROPEAN JOURNAL OF NEUROSCIENCE, 1998, V10, N8 (AUG), P2607-2616
ISSN: 0953-816X Publication date: 19980800
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND
Language: English Document Type: ARTICLE
Abstract: Members of **arrestin** /beta- **arrestin** protein family are thought to participate in agonist-mediated desensitization of G-protein-coupled receptors, including rhodopsin and beta(2)-adrenergic receptor. Unlike in human and cow, splice variants of this protein family in rat have not been studied extensively, and there has been no report on their existence at protein level. Hence, a previous report by others on the localization of both beta- **arrestin** -1 and -2 in a wide range of innervated rat tissues could imply their broad receptor specificity. In this report we show the presence of two alternatively spliced forms of beta- **arrestin** -1 in several rat tissues using both reverse transcription-polymerase chain reaction and Western immunoblot. Splicing of beta- **arrestin** -1 pre-mRNA appears to be subject to differential regulation between the rat CNS and peripheral tissues. In contrast, we **detected** no splice variants of beta- **arrestin** -2 in rat. A comparison of the genomic DNA sequences of bovine and rat beta- **arrestin** -2, where the splicing of bovine beta- **arrestin** -2 mRNA has been reported, revealed a high degree of homology in their organization of exons and introns as well as certain differences that might be responsible for the different processing of beta- **arrestin** -2 mRNA in the two species. Our two-dimensional isoelectric focusing gels using rat spinal cord and heart tissues demonstrate isoelectric heterogeneity of rat beta- **arrestin** -1, suggesting that beta- **arrestin** -1 is subject

to post-translational modification unlike beta- **arrestin** -2.

6/3,AB/8 (Item 1 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online

01721907 AADAAI9953532
Effects of phosphorylation **of rhodopsin's active state equilbrium and its interactions with G protein and** arrestin
Author: Gibson, Scott Keven
Degree: Ph.D.
Year: 1999
Corporate Source/Institution: University of Pennsylvania (0175)
Source: VOLUME 60/12-B OF DISSERTATION ABSTRACTS INTERNATIONAL. PAGE 6083. 157 PAGES

Deactivation of many G protein coupled receptors (GPCRs) is known to require **phosphorylation** of the activated receptor. **Phosphorylation** reduces the rate of G protein activation and allows the binding of the inhibitory protein **arrestin** . Receptor **phosphorylation** stoichiometries as high as nine have been **detected** in vitro; however, it is not known how many **phosphorylation** sites can modulate **GPCR** activity and are physiologically relevant. In this study, we take advantage of the unique spectroscopic properties of the **GPCR** rhodopsin to measure the effect of **phosphorylation** on the receptor and its interactions with G protein and **arrestin** .

Upon light-activation, rhodopsin forms an intramolecular equilibrium between two conformers, metarhodopsin I and II (MI and MII). We find surprisingly that increasing rhodopsin **phosphorylation** stoichiometry augments rather than diminishes the formation of MII, the conformation that activates G protein. We show that **phosphorylation** increases the apparent pK for MII formation. Decreasing ionic strength enhances this effect. Gouy-Chapman theory shows that the change in pK is quantitatively explained by the membrane surface potential, which becomes more negative with increasing **phosphorylation** stoichiometry and decreasing ionic strength. This lowers the membrane surface pH compared to the bulk pH, increasing the MI–MII equilibrium constant toward MII and the rate of MI formation (k₁), while decreasing the back rate constant (k_{−1}) of the MI–MII relaxation.

Increasing rhodopsin **phosphorylation** stoichiometries also increased **arrestin** affinity while weakening G protein affinity. **Arrestin** binding was favored over G protein binding at **phosphorylation** stoichiometries greater than two. The effect of **phosphorylation** on the binding affinity of G protein and **arrestin** was attenuated at high ionic strength. This ionic strength effect suggests that **phosphorylation** electrostatically modulates **arrestin** and G protein binding.

6/3,AB/9 (Item 1 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text

04512169 H.W. WILSON RECORD NUMBER: BGSA01012169
Regulation of phosphoinositide-specific phospholipase C.
Rhee, Sue Goo
Annual Review of Biochemistry v. 70 (2001) p. 281-312
SPECIAL FEATURES: bibl il ISSN: 0066-4154
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
WORD COUNT: 13217

ABSTRACT: Eleven distinct isoforms of phosphoinositide-specific phospholipase C (PLC), which are grouped into four subfamilies (b, c, d, and e), have been identified in mammals. These isozymes catalyze the hydrolysis of phosphatidylinositol 4,5-bisphosphate {PtdIns(4,5)P2} to inositol 1,4,5-trisphosphate and diacylglycerol in response to the

activation of more than 100 different cell surface receptors. All PLC isoforms contain X and Y domains, which form the catalytic core, as well as various combinations of regulatory domains that are common to many other signaling proteins. These regulatory domains serve to target PLC isozymes to the vicinity of their substrate or activators through protein-protein or protein-lipid interactions. These domains (with their binding partners in parentheses or brackets) include the pleckstrin homology (PH) domain {PtdIns(3)P, bc subunits of G proteins} and the COOH-terminal region including the C2 domain (GTP-bound a subunit of Gq) of PLC-b; the PH domain {PtdIns(3,4,5)P3} and Src homology 2 domain {tyrosine- **phosphorylated** proteins, PtdIns(3,4,5)P3} of PLC-c; the PH domain {PtdIns(4,5)P2} and C2 domain (Ca2+) of PLC-d: and the Ras binding domain (GTP-bound Ras) of PLC-e. The presence of distinct regulatory domains in PLC isoforms renders them susceptible to different modes of activation. Given that the partners that interact with these regulatory domains of PLC isozymes are generated or eliminated in specific regions of the cell in response to changes in receptor status, the activation and deactivation of each PLC isoform are likely highly regulated processes. Reprinted by permission of the publisher.

6/3,AB/10 (Item 2 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text

04265309 H.W. WILSON RECORD NUMBER: BGSA00015309
Intrarenal dopamine: a key signal in the interactive regulation of sodium metabolism.
Aperia, Anita C
Annual Review of Physiology v. 62 (2000) p. 621-47
SPECIAL FEATURES: bibl il ISSN: 0066-4278
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
WORD COUNT: 11700

ABSTRACT: The kidney regulates sodium metabolism with extraordinary precision and sensitivity. This is accomplished by an intricate interaction between signals from extrarenal and intrarenal sources and between anti-natriuretic and natriuretic factors. Dopamine, produced in renal proximal tubule cells, plays a central role in this interactive network. Natriuretic hormones that are released from extrarenal sources, such as atrial natriuretic peptide, mediate some of their effects via renal dopamine receptors. On the level of the tubules, dopamine acts by opposing the effects of anti-natriuretic factors, such as angiotensin II and a-adrenergic receptors. Sodium retention leads to an increase in renal dopamine tonus, and the natriuretic effects of dopamine are more prominent under this condition. Inhibition or down-regulation of dopamine receptors significantly attenuates the natriuretic response to salt loading. Renal dopamine is modulated by the supply of filtered L-DOPA and the metabolism of dopamine via catechol-O-methyldopamine. The importance of dopamine as a natriuretic hormone is reflected by its capacity to inhibit the majority of renal tubule sodium transporters. Notably, the activity of Na+,K+ATPase is inhibited in most tubule segments by dopamine. Recent studies have elucidated many of the signaling pathways for renal dopamine receptors. Novel principles for homologous and heterologous sensitization of dopamine receptors have been **detected** that may explain some of the interaction between dopamine and other first messengers that modulate renal tubule sodium transport. A broad understanding of the renal dopamine system has become increasingly important, since there is now strong evidence from both clinical and experimental studies that dysregulation of the renal dopamine system plays a role in many forms of multigenetic hypertension. With permission, from the Annual Review of Physiology Volume 62, 2000, by Annual Reviews Inc. (http://www.annurev.org).

6/3,AB/11 (Item 3 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text

03546766 H.W. WILSON RECORD NUMBER: BGSA97046766

Clathrin-coated vesicle formation and protein sorting: an integrated process.

Schmid, Sandra L

Annual Review of Biochemistry v. 66 (1997) p. 511-48
SPECIAL FEATURES: bibl il ISSN: 0066-4154
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
WORD COUNT: 16676

ABSTRACT: Clathrin-coated vesicles were the first discovered and remain the most extensively characterized transport vesicles. They mediate endocytosis of transmembrane receptors and transport of newly synthesized lysosomal hydrolases from the trans-Golgi network to the lysosome. Cell-free assays for coat assembly, membrane binding, and coated vesicle budding have provided detailed functional and structural information about how the major coat constituents, clathrin and the adaptor protein complexes, interact with each other, with membranes, and with the sorting signals found on cargo molecules. Coat constituents not only serve to shape the budding vesicle, but also play a direct role in the packaging of cargo, suggesting that protein sorting and vesicle budding are functionally integrated. The functional interplay between the coated vesicle machinery and its cargo could ensure sorting fidelity and packaging efficiency and might enable modulation of vesicular trafficking in response to demand.

6/3,AB/12 (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01721513 SUPPLIER NUMBER: 19825775 (USE FORMAT 7 OR 9 FOR FULL TEXT)

Role of the glucagon receptor COOH-terminal domain in glucagon-mediated signaling and receptor internalization.

Buggy, Joseph J.; Heurich, Rainer O.; MacDougall, Margit; Kelley, Keith A.; Livingston, James N.; Yoo-Warren, Heeja; Rossomando, Anthony J.

Diabetes, v46, n9, p1400(6)
Sep,
1997
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0012-1797
LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 5112 LINE COUNT: 00435

6/3,AB/13 (Item 1 from file: 370)
DIALOG(R)File 370:Science

00508752

beta) - Arrestin -Dependent Formation of (beta) .inf(2) Adrenergic Receptor-Src Protein Kinase **Complexes**

Luttrell, L. M.; Ferguson, S. S. G.; Daaka, Y.; Miller, W. E.; Maudsley, S. ; Della Rocca, G. J.; Lin, F.-T.; Kawakatsu, H.; Owada, K.; Luttrell, D. K.; Caron, M. G.; Lefkowitz, R. J.
L. M. Luttrell, Y. Daaka, W. E. Miller, S. Maudsley, G. J. Della Rocca, F.-T. Lin, M. G. Caron, and R. J. Lefkowitz are at the Howard Hughes Medical Institute and Departments of Medicine, Surgery, Biochemistry, and Cell Biology, Box 3821, Duke University Medical Center, Durham, NC 27710, USA. S. S. G. Ferguson is at the John P. Robarts Research Institute, Post Office Box 5015, 100 Perth Drive, London, Ontario N6A 5K8, Canada. H. Kawakatsu is at the Lung Biology Center, University of California, Box 0854, San Francisco, CA 94143, USA. K. Owada is at the Institute for Molecular and Cellular Biology, Kyoto Pharmaceutical University, 1 Shichono-cho, Misasagi, Yamashina-ku, Kyoto 607, Japan. D. K. Luttrell is

in the Department of Molecular Biochemistry, Glaxo Wellcome Research and Development, Research Triangle Park, NC 27709, USA.
Science Vol. 283 5402 pp. 655
Publication Date: 1-29-1999 (990129) Publication Year: 1999
Document Type: Journal ISSN: 0036-8075
Language: English
Section Heading: Research Article
Word Count: 4495

Abstract: The Ras-dependent activation of mitogen-activated protein (MAP) **kinase** pathways by many receptors coupled to heterotrimeric guanine nucleotide binding proteins (G proteins) requires the activation of Src family tyrosine kinases. Stimulation of (beta) .inf(2) adrenergic receptors resulted in the assembly of a protein complex containing activated c-Src and the receptor. Src recruitment was mediated by (beta) - **arrestin** , which functions as an adapter protein, binding both c-Src and the agonist-occupied receptor. (beta) - **Arrestin** 1 mutants, impaired either in c-Src binding or in the ability to target receptors to clathrin-coated pits, acted as dominant negative inhibitors of (beta) .inf(2) adrenergic receptor-mediated activation of the MAP kinases Erk1 and Erk2. These data suggest that (beta) - **arrestin** binding, which terminates receptor-G protein coupling, also initiates a second wave of signal transduction in which the "desensitized" receptor functions as a critical structural component of a mitogenic signaling complex